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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,075	11/26/2003	Jo Klaveness	NIDN-10311 CON	6312

7590 10/11/2006

Li CAI
Amersham Health, Inc.
101 Carnegie Center
Princeton, NJ 08540-6231

EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,075	KLAVENESS ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 38-44 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 38-44 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 11/26/2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/959,206.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 11/26/2003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Double Patenting

Claims 38 – 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 5 and 8 – 10 of U.S. Patent No. 6,261,537. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to a targetable agent comprising gas-filled microbubbles, a film-forming surfactant comprising phospholipids, a peptide linker, and a vector which is associated with angiogenesis or atherosclerotic plaques and/or thrombi. Accordingly, the scope of the pending claims overlaps with that of the patented claims, and thus they are obvious variants of the patented claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38 – 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 6,139,819, which is a Continuation-in-part of US 08/640,464, filed May 1, 1996 and of US 08/497,684 filed June 7, 1995. The parent applications were checked and were found to encompass the same subject matter as the '819 patent as described herein) in view of Unger (US 5,656,211).

Unger discloses targeted contrast agents for diagnostic and therapeutic use in the '819 patent. The contrast agent comprises, in an aqueous carrier, a phospholipid and a gas, in combination with a targeting ligand (abstract and claims 1 and 2). The gas may be selected from the group consisting of sulfur hexafluoride, perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane (claims 1 and 13). In the preferred form, the lipid may be a monolayer or bilayer (column 7, line 36 – 37). The phospholipids are selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, and phosphatidic acid, for example (claims 1 – 3). The compositions further comprise a targeting ligand, and the targets preferably recognize atherosclerotic plaques (column 47, line 65). Additionally, Unger teaches that a variety of targeting ligands are suitable, i.e. for targeting myocardial cells, including endothelin as claimed (column 38, line 61). The targeting ligands are

preferably associated with the lipid compounds covalently or non-covalently (column 34, lines 24 – 28). The targeting agent is preferably a protein or peptide (column 34, lines 59 – 66), and when the protein or peptide target is covalently bound to the lipid, it is interpreted to be within the scope of the instant limitation that a linker comprises a "peptide linker portion" because there is inherently a portion of a peptide linked to the phospholipids. In addition to the diagnostic benefits which the methods and compositions of Unger may provide, the composition may also be employed to administer bioactive agents, including therapeutic materials. The bioactive agents may include hormones, antibiotics, etc. (column 16, line 18 – 42). The targeting materials may also be therapeutic (i.e. vitamins), and may include disulfide bonds (column 14, line 3).

In the '211 patent, Unger teaches similar contrast agent vesicles which comprise a gas and a monolayer or bilayer of phospholipids (i.e. phosphatidylcholines, etc.) which may bear peptides or proteins or charged amino acids such as polylysine or polyarginine. These targeting or binding compounds may be specifically chemically attached to the lipids (column 6, lines 1 – 30). Thus, it is interpreted that the target is linked to the lipid via a peptide portion. Therapeutic materials (i.e. pharmaceuticals) may also be incorporated (column 11, line 21), although it is not specified that they are covalently linked to the reporter via disulfide bonds.

Unger does not teach that the targeting agent should be associated with atherosclerotic plaques in the '211 patent.

Contrast agents comprising phospholipid liposomes in an aqueous carrier which encapsulate a fluorinated gas, and which further bear a target that is preferably peptide or protein which may be covalently associated with the lipid, and may recognize atherosclerotic plaques, were taught by Unger to be useful for diagnostic and therapeutic uses. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize a

portion of a peptide to link a target that binds sites associated with angiogenesis to a phospholipid surfactant with a reasonable expectation of success because peptide targets (which may recognize atherosclerotic plaques) have been shown to be linked to phospholipids by Unger. Motivation to use the atherosclerotic plaque-targeting agents was also taught by Unger, because gas filled vesicles targeted to atherosclerotic plaque are useful to non-invasively detect diseased blood vessels before severe damage has occurred, for example, prior to stroke or myocardial infarction, so that appropriate medical or surgical intervention may be implemented (column 36, lines 64+). Unger also taught the combination of therapeutics with the targeted diagnostic agents, including via disulfide bonds.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lhs

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER